

## Chill as a Side Effect of Atomoxetine Use: Case Report

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### Abstract

Atomoxetine is a non-stimulatory treatment option with FDA approval for the treatment of ADHD as a selective inhibitor of presynaptic norepinephrine carriers in the central nervous system. The most common side effects reported in children and adolescents are abdominal pain, decreased appetite, vomiting, drowsiness, nervousness, weakness, dizziness, and dyspepsia; other more uncommon side effects are also observed. The treatment of a 7-year-old child diagnosed with ADHD has been replaced with atomoxetine due to loss of appetite and weight loss developing with the initiation of stimulant treatment. A rare chill side effect has been reported after atomoxetine treatment. To our knowledge, this is the first case that atomoxetine-related chill side effect has been reported.

**Keywords:** Treatment; Behaviors; Inhibitory; Trauma; Psychiatric

### Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a very common disorder with a prevalence of 5-10% in childhood and 4% in adulthood [1]; it is characterized by a shortness of duration of permanent and constant attention, and impetuosity and restlessness in behaviors or cognition due to the lack of inhibitory control. As a result, there is carelessness or hyperactivity that does not fit into the developmental period of the child. While the onset is usually around the age of three, the diagnosis is made during the primary school years, in which development of the concentration and the attention period essential for the formal education are expected. Research results on the prevalence of ADHD differ depending on the identification of cases in particular [2].

Atomoxetine is a non-stimulant treatment option approved by the FDA (Food and Drug Administration) for the treatment of ADHD as a selective inhibitor of presynaptic norepinephrine carriers in the central nervous system [3]. The most common side effects reported in children and adolescents are abdominal pain, decreased appetite, vomiting, drowsiness, irritability, weakness, dizziness and dyspepsia [4-6].

In this article, we presented a case where 7-year-old boy, who had symptoms of ADHD and treated with atomoxetine, has shown symptoms of chill from the first day of treatment.

### Case Presentation

A seven-year-old boy was brought by his parents to our clinic with complaints of "hyperactivity, not listening to lessons in class, not wanting to do homework, distractibility, not attending to his possessions and impatience". From his history, it was understood that these complaints have existed since the age of 3-4, that the teachers expressed similar complaints when he attended the nursery and preschool, and that his problems became worse especially during the first semester of primary school. In his background, it was stated that there was no problem in his motor-mental development stages, he had no epileptic seizure/trauma or any other significant illness, he learned to read and write on time, and he is an animated and talkative child in general. There was nothing of significance in the family history.

His psychiatric assessment has shown that the psychomotor activity was increased and the impulsivity was prominent. There were no other psychiatric findings. His physical and neurological examinations were normal. As a result of psychiatric evaluations, ADHD-hyperactivity-impulsivity was considered to be the predominant type according to DSM-V diagnostic criteria.

Due to his existing complaints that impaired the school adaptation and performance, a treatment was started with the initial dose of long-acting methylphenidate 18 mg and the dosage was increased at follow-ups since the response to medicine was insufficient. However, a marked decrease in appetite was observed with the use of methylphenidate 27 mg, leading to weight loss. In the course of this treatment, which lasted for about a month, the lack of appetite continued in the same way, and thus, a treatment change was planned. Atomoxetine 18 mg was administered and it was planned to increase the dosage gradually. Together with the use of atomoxetine, the mother told that the child was cold during the day, wanted to sleep, and wanted to be covered. It was stated that the complaint has continued during the time of atomoxetine use when the outside temperature was 35-40°C and the patient had no infection. It was stated that the patient was cold after 1-2 hours of taking the medicine and the complaints diminished or disappeared after sleeping for 1-2 hours. On the next follow-up visit, the dosage was increased as planned and the medication time was changed to before bedtime. It was found that the chill side effect decreased during the daytime and was never seen on some days after this change. It was planned to continue with the same dosage, to observe the patient for a time, and to assess the atomoxetine dosage since there was partial improvement in ADHD symptom and functioning of the patient and a visible decrease in the side effect was observed with changing the medication time.

### Discussion

In this article, a case was reported involving a 7-year-old boy, who was diagnosed with ADHD and discontinued the medical treatment due to loss of appetite and weight loss in connection with stimulant but developed an uncommon chill side effect with alternative atomoxetine treatment.

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Atomoxetine is an agent that inhibits presynaptic norepinephrine transport with minimal affinity to other neuronal signaling pathways. It is thought that the pathogenesis of ADHD is related to anomalies in catecholamines such as dopamine and norepinephrine prefrontal cortex [7]. Thus, synaptic and extracellular norepinephrine levels induced by atomoxetine improve the clinical symptoms of ADHD such as the lack of attention.

Side effects including abdominal pain, vomiting, headache, constipation, nausea, loss of appetite, depressive mood, irritability, cardiac murmur, QT prolongation, hypertension, tachycardia, and wolf-parkinson-white syndrome have been reported in association with the use of atomoxetine [8-10].

In addition to the common side effects, rare side effects were also encountered. In our literature study, it was found that there were cases of angioedema, separation anxiety, hair loss, vitiligo, atopic dermatitis, urinary retention, and raynaud phenomenon due to the use of atomoxetine [11-17].

## Conclusion

In this case study, the facts that the clinical evaluations are normal, the patient did not use medicines other than atomoxetine, the side effect decreased significantly with changing the medication time to night time excludes secondary causes and suggests that this side effect may be due to the use of atomoxetine.

Atomoxetine affects through increasing the dopamine and noradrenaline levels by inhibiting the norepinephrine transporters in the prefrontal cortex [18]. Although it is not known which mechanism of atomoxetine leads to the cold side effect, it is suggested that it is because atomoxetine induces and increases noradrenaline levels in peripheral and central synapses, and this, in turn, induces peripheral alpha 1 and alpha 2 receptors and leads to prolonged vasoconstriction [19,20].

The fact that there is no evidence of atomoxetine-induced chill side effects in children with ADHD in the literature suggests that this represents the first such case. We think that it would be appropriate for the clinician to evaluate with the possibility of this side effect in mind.

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